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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,119	02/10/2004	John D. Mountz	UAB-11703/22	5461

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,119	MOUNTZ ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the restriction/election requirement received on 8/28/06 has been entered. Claims 1-21 are pending in the instant application. Applicant's election without traverse of the species "adenovirus" as the vector and "CFTR" as the transgene is acknowledged. Claims 1-21 read on the elected species and are currently under examination in the instant application. An action the merits follows.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 3/25/04 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner and an initialed and signed copy is attached to this action.

Please note, that the listing of references on pages 51-55 in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to methods for promoting immunotolerance in a host comprising transfecting a host cell with a vector that expresses a transgene, an antigen, and a Fas 2 ligand. The specification does not provide sufficient written description for a "Fas 2 ligand". The specification is primarily focused on the use of Fas ligand, also known as CD95 ligand or CD178, in the instant invention as claimed and provides scant reference to a Fas 2 ligand. The specification does not actually refer to a "Fas 2 ligand" but instead contains a single sentence on page 15, which states, "Other such ligands illustratively include: Fas ligand 2 which induces apoptosis by acting with death domain region molecules DR3, DR4 and DR5; TNF which induces apoptosis by acting with TNFRI; Granzyme B and porferin which are natural killing molecules associated with T-cells; and antibodies specific to T-cell apoptosis ligand receptors: anti-Fas, anti-DR3, anti-DR4, anti-DR5 and anti-TNFR 1" (emphasis added by examiner); and a single sentence on page 18, which states, "For example, the nucleic acid sequences coding for Fas ligand, Fas ligand 2, Granzyme B and porferin can be altered by

substitutions, additions, deletions or multimeric expression that provide for functionally equivalent ligands.". It is unclear whether the "Fas 2 ligand" recited in the claims and the "Fas ligand 2" recited in the specification are in fact the same molecule. Further, the specification does not provide any nucleic acid sequence information for a Fas 2 ligand or Fas ligand 2 derived from any species of animal, or provide any description of how or from what source such a nucleic acid sequence can be or has been obtained, or provide the structural or chemical properties of such a molecule. In addition, a thorough search of several commercially and publicly available databases yielded no results which teach a "Fas 2 ligand" or "Fas ligand 2" or any abbreviations thereof. A further search of the NCBI database did not identify any nucleic acid sequence known as "Fas 2 ligand' or "Fas ligand 2". While it is common that molecules may be referred to by several different titles or symbols, the specification fails to give any alternative titles for "Fas 2 ligand", and neither the prior art nor post-filing art identifies any molecule which is also known as "Fas 2 ligand" or "Fas ligand 2". The only information given in the specification refers to the ability of "Fas 2 ligand" to induce apoptosis through DR3, DR4, and DR5. However, the prior art does not teach a single molecule referred to as "Fas ligand 2" or "Fas 2 ligand" capable of binding to all three of DR3, DR4, and DR5. The prior art teaches that DR5 (also known as TRAILR2, KILLER, or TRICK2) is the receptor for TRAIL (also known as APO2L). The prior art also teaches that TRAIL also binds to DR4 (also known as TRAILR1). However, there is no suggestion in the prior art that TRAIL is known as "Fas 2 ligand". As such, neither the specification nor the prior art provides any actual description of a nucleic acid sequence known as "Fas 2 ligand", much less provide guidance as to particular properties of any such molecule from any animal.. In the absence of such description, the skilled artisan cannot

envision the detailed chemical structure of any nucleotide sequence which encodes "Fas 2 ligand" and thus cannot envision the detailed chemical structure of any adenoviral vector comprising a "Fas 2 ligand" encoding nucleic acid.

It is further noted that since the specification fails to provide adequate written description for the detailed chemical structure and properties of "Fas 2 ligand", the specification further fails to provide sufficient written description for any second ligand that "induces apoptosis of said T-cell by the same mechanism as said Fas 2 ligand". The specification does not specifically teach the mechanism by which "Fas 2 ligand" induces apoptosis, and further does not identify any molecule that induces apoptosis of T cells using the same mechanism as "Fas 2 ligand".

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is claimed." (See page 1117). The instant specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may also be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession

of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). The applicant has not provided any description or reduction to practice of a nucleic acid encoding "Fas 2 ligand" or any ligand that induces apoptosis by the same mechanism as "Fas 2 ligand". Based on the applicant's specification, the skilled artisan cannot envision the detailed chemical structure of the nucleotide sequences which encode any "Fas 2 ligand" from any animal species. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel,* 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016. Thus, for the reasons outlined above, claims 1-21 do not meet the requirements for written description under 35 U.S.C. 112, first paragraph.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to provide an enabling disclosure for making, isolating, or using a nucleic acid encoding a "Fas 2 ligand" from any species of animal. As discussed in substantial detail in the rejection of the claims for lack of written description above, the specification only

contains 2 references to a "Fas ligand 2" on pages 15 and 18. The specification does not disclose any nucleic acid sequence encoding a "Fas 2 ligand" from any animal species, provide any guidance that nucleic acid sequences encoding a "Fas 2 ligand" were known in the prior art, or provide any of the necessary guidance to isolate such a nucleic acid *de* novo from any genomic or cDNA library. The specification is further silent as to specific physical and functional properties of a "Fas 2 ligand". Further as discussed above, neither the prior nor post-filing art makes any reference to a "Fas 2 ligand" or "Fas ligand 2" or provides any indication that any other known molecule is or has been referred to in the alternative as "Fas 2 ligand". In the absence of any such information, it would require undue experimentation to isolate or identify a nucleic acid molecule encoding a "Fas 2 ligand" for use in the claimed methods.

In addition, claim 3 refers to a second vector expressing a second ligand that "induces apoptosis of said T-cell by the same mechanism as said Fas 2 ligand". While various ligands were known in the art at the time of filing that were capable of inducing apoptosis, the specification fails to provide sufficient guidance for identifying which of these ligand share the same mechanism for inducing apoptosis as "Fas 2 ligand". The single sentence on page 15 of the specification regarding the activity of "Fas ligand 2", assuming *arguendo* that this is the same as "Fas 2 ligand", simply states that Fas ligand 2 induces apoptosis by acting with death domain region molecules DR3, DR4 and DR5. This sentence, however, does not provide any specific information concerning the mechanism of apoptosis induction in T cells. The sentence does not indicate whether "Fas ligand 2" binds to all three of these molecules or somehow causes the activation or production of other molecules that in turn bind to DR3, DR4, and DR5. Since the mechanism by which "Fas 2 ligand" induces apoptosis in T cells is not specifically disclosed in

the specification, it would require undue experimentation for the skilled artisan to identify or isolate additional putative ligands which share the exact same mechanism of inducing apoptosis in T cells as "Fas 2 ligand".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5, and 7-13 are confusing and appears to omit essential method steps. Claim recite contains a single method step comprising "transfecting a host cell with said vector". While the preamble states that the method is for promoting immunotolerance in a host. The single method step is not limited to the transfection of a host cell *in vivo* in said host. The claim appears to read on transfection of the host cell *in vitro* or *in vivo*. This interpretation is supported by dependent claim 5 which recites that the transfecting occurs *in vitro*. The *in vitro* embodiment encompassed by claim 1 and specifically recited by claim 5 lacks the essential method step wherein the transfected host cell is administered to the host such that immunotolerance could occur. Note that claims 2-4, and 7-13 are also included in this rejection as they depend on claim 1.

Applicant is advised that should claim 9 be found allowable, claim 10 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Note that the vector of claim 1 comprises a transgene, an antigen, and Fas 2 ligand, and thus is already "recombinant".

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your

application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER